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EXAMINER

LEAVITT, MARIA GOMEZ

ART UNIT	PAPER NUMBER
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1633

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/21/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/509,444	REID ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Maria Leavitt	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 22 November 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-19 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 09-28-2004 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>03-21-2005</u>  | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Claims 1-19 are pending. Applicant's election **with traverse** of the following species in the reply filed 12-22-2006 in response to the restriction/election requirements is acknowledged: urogenital flora as specifically named bacteria flora, *L. rhamnosus* as specifically named second probiotic organism and oral administration as specifically named method of administration.

### ***Response to arguments***

On page 4 of Applicant's Response to the Restriction Requirements, Applicant argues that administration of species of different second probiotic organism employs the same inventive concept as and technical features of the present invention. Moreover, applicant argues that oral and vaginal administration routes are merely two different aspects in employing the same single concept of the present invention. The comments are found persuasive. As such species election of a second probiotic organism and a specifically named method of administration is withdrawn. However, Applicant's traversal to species election of a specifically named bacteria flora has not been found persuasive.

On page 4 of applicant's remarks, applicant states "establishing gastrointestinal or urogenital flora in females throughout life by administering a therapeutically effective amount of at least one *Lactobacillus iners* are two different ways to the establishment and maintenance of a healthy urogenital flora". Such is not persuasive.

As stated in the previous office action, the urogenital microbiota and gastrointestinal microbiota comprise different microorganism with different structure and functionality, with domination of different strains being influenced by many factors. For example, enzymes

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produced by micro flora of the small intestine specifically digest food substances (e.g., maltase, lactase, fats) while they are being absorbed through the epithelium.

Therefore claims 1-19 are currently pending for examination to which the following grounds of rejection are applicable.

### *Nature of the inventions*

The present invention is drawn to a method for establishing a healthy vaginal bacterial flora in females by administration of a therapeutically effective amount of at least one *Lactobacillus iners* in a pharmaceutically acceptable carrier. Moreover, the instant invention is to the administration of an additional second probiotic organism.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 claims insulin as a prebiotic. A "prebiotic" is defined in the specification as "a nonmetabolized, nonabsorbed substrate that is useful for the host which selectively enhances the growth and/or the metabolic activity of a bacterium or a group of bacteria. A prebiotic also

includes a nutrient utilized by lactobacilli or bifidobacteria to stimulate and/or enhance growth of lactobacilli or bifidobacteria relative to pathogenic bacteria” p. 5. Moreover, the as-filed specification teaches of “inulin” as a prefer prebiotic. Hence, it is unclear how insulin relates to inulin as a prebiotic.

For the purpose of a compact prosecution, the prebiotic claimed in claims 17 is interpreted as “inulin”.

***Claim Rejections - 35 USC § 112- First paragraph- Scope of Enablement***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-8, 13-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification is enabling only for claims limited to:

A method of inhibiting urogenital pathogens colonization of the urogenital tract in women comprising orally administering a therapeutically effective amount of at least one *Lactobacillus iners* and a pharmaceutically acceptable carrier.

The specification does not reasonably provide enablement for a method of maintaining a healthy urogenital flora in females by administering a therapeutically effective amount of at least one *L. iners* by any route of administration. Moreover, the specification does not reasonably provide enablement for a method of treatment of any infection in a subject as broadly embraced by claim 19.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

“Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.”

Claims 1-8, 13-19 when given the broadest reasonable interpretation encompass a method for maintaining a healthy urogenital flora in females by administering a therapeutically effective amount of at least one *L. iners* by any route of administration, including parenteral (e.g., intramuscular, intracardiac, subcutaneous, intraperitoneal, intravenous), topical, and enteral (e.g., mouth) routes. Specific issues of distribution and generation of immunity in the mucosal urogenital flora have to be considered for the different modes of administration of a pharmaceutically acceptable carrier comprising *L. inners*. The as-filed specification discloses that 19 non-symptomatic women were studied to investigate the effect and persistence of vaginally inserted capsules administered for three days containing viable *lactobacilli*: *L. fermentum* RC-14 and *L. rhamnosus* GR-1 (p. 19). However, no other data is disclosed about administration of viable lactobacilli by any other route. Prior art (Reid et al., FEMS Immunology and Medical Microbiology, 2001, 37-41; p. 40, columns 1 and 2) teaches successful maintenance of a normal vaginal flora after oral ingestion of capsules comprising  $10^8$  viable probiotic lactobacilli (Reid et al., FEMS Immunology and Medical Microbiology, 2001, 37-41; p. 40, columns 1 and 2). Similarly, Sobel (Bacterial vaginosis. *Annu Rev Med.*

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2000;51:349-56 ) teaches successful oral and topical therapy for the treatment of bacterial vaginosis (p. 354). In contrast, Russell-Jones (Journal of Controlled Release, 2000, 49-54) discloses that parenteral route of administration of vaccines does not extend immunity to the mucosal surfaces, and production of these antibodies can only be generated through mucosal delivery of the antigen or vaccine or by oral administration (p. 49, col. 2; p. 52, col. 2). The as-filed specification does not provide sufficient guidance for any method of administration other than vaginally inserted capsules containing viable *lactobacilli*. As the result, given the unpredictability of the art and the lack of working example in the instant specification in relation to using any route of administration, particularly when taken with the lack of guidance in the specification, it would have required undue experimentation to practice the instant method to identify an enormous number of methods of routes of administration for maintaining and/or establishing a healthy urogenital flora in females as broadly claimed other than oral or topical administration. .

Claim 19 when given the broadest reasonably interpretation, encompasses methods for treatment of any infection in a subject, including a human subject. Thus claim 19 can be interpreted as a method for treatment of virtually every infectious disease transmitted by bacteria, viruses, fungi and protozoa, including upper respiratory tract infections (e.g., common cold caused by rhinoviruses, influenza viruses, adenovirus; diphtheria , bacterial pneumonia), urinary tract infections (e.g., Enterobacteriaceae such as Enterobacter, Serratia, Pseudomonas, Staphylococcus), obstetric and perinatal infections (e.g, malaria, viral hepatitis, poliomyelitis, polyomavirus, HIV, cytomegalovirus), sexually transmitted diseases (e.g., papillomaviruses, Chlamydia, Herpes simplex virus types 1 and 2, HIV), lymphomas and leukemias cancer caused

by HTLV1 and HTLV2. These are widely divergent diseases in terms of their pathologic mechanisms. For example, the treatment diphtheria caused by a toxin-producing strain of *C. diphtheriae* uses antitoxin and antibiotics (Mims et al., Medical Microbiology, third edition, 2004, p. 214-215); similarly urinary tract infections caused by bacteria are treated with oral antibacterial (e.g., ampicilin, amoxicillin, trimethoprin) (Mims et al., 2004, pp. 246-247). In contrast, certain viruses can cause permanent malignant changes in cells such as HTV1 and 2 (lymphomas, leukemias), Epstein-Bar virus (nasopharyngeal carcinoma), genital papilloma viruses (cervical cancer) and heptatis B virus (liver cancer)( Mims et al., 2004; pp. 194-196) wherein clinical treatment have had limited success. For example, antiretrovial therapy has been used for the treatment of AIDS since 1990 with improvements in disease prognosis but still there is not cure for the disease, furthermore appearance of drug-resistant HIV viruses affects the efficacy of subsequent retroviral therapy (Mims et al., 2004; pp. 270-271). Similarly, there is not effective, though treatment for HTLV1 infection, antiroretrovial agents are shown to inhibit viral replication (Mims et al., 2004; p. 380). Therefore, it seems likely that a cellular treatment of a cell population that is an effective treatment with antibiotics for infectious diseases caused by a bacteria such as diphtheria , would unlikely be effective at treating sexually transmitted diseases such as cervical cancer, or AIDS . The as-filed specification teaches examination of vaginal bacterial microrbiota of 20 non-symptomatic women by PCR-denaturing gradient gel electrophoresis (DGGE) and sequencing the V2-V3 region of the 16S rRNA (p. 14, Example 1, p. 17). Moreover, 19 non-symptomatic women were studied to investigate the effect and persistence of vaginally inserted capsules administered for three days containing viable *lactobacilli*: *L. fermentum* RC-14 and *L. rhamnosus* GR-1 (p. 19). Vaginal samples of the 19



women studied had a relatively “simple” bacteria flora represented by one of three fragments observed by PCR-DGGE analysis. The majority of the woman tested (15/19) had a least one sequence homologous to *L. iners*. Moreover, the exogenous strains could be detected for up to 21 days in some subjects. Further, the specification concludes that the PCR-DGGE has provided a means to develop understanding of microorganisms within the vagina and showed that non-peroxide producing *L. rhamnosus* GR-1 colonizes better than *L. fermentum* RC-14 (p.24) . However, the application is silent about any treatment of any infection other than inhibiting urogenital pathogens colonization of the urogenital tract by combination therapy of Lactobacilli.

Hence, it is clear that the treatment of these widely divergent diseases is highly complex, and requires consideration of numerous factors. In contrast the instant specification has only provide a limited *in vivo* characterization of the improved understanding of the bacterial vaginal flora of woman before and after probiotic installation with capsules of *L. rhamnosus* GR-1 and *L. fermentum* RC-14; further contemplating the advantages of a combination therapy in some women for clinical studies of the vaginal tract. Thus, given the unpredictability of the art and the lack of working example in the instant specification, one of ordinary skill in the art is no enable to make and use a therapeutic effective amount of *Lactobacillus iners* for the treatment of a disease in a human subject, as broadly claimed.

#### ***Claim Rejections - 35 USC § 102***

Claim 15 is drawn to a pharmaceutical composition comprising *L. iners* and a pharmaceutically acceptable carrier. The as-filed specification defines a “pharmaceutically-acceptable carrier” as any one or more compatible solid or liquid able of being commingled

without substantially decreasing the pharmaceutical efficacy of the composition (p. 11). Thus the pharmaceutical composition can be broadly interpreted as any media that comprises *L. iners* without affecting the efficacy of the composition.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 15 is rejected under 35 U.S.C. 102(e) as being anticipated by Falsen et al., Journal of Systematic Bacteriology, 1999, 217-221.

Falsen et al., teaches a new isolated species of Lactobacillus: *L. inners* that grows in an agar culture supplemented with 5% horse blood at 37C in air plus CO<sub>2</sub>. Moreover, the preparations of whole protein extract comprising *L. inner* is used for densitometric analysis (p. 218, col. 1)

Thus by teaching all the limitations of claim 15, Falsen et al., anticipates the instant invention.

### ***Rejection, Obviousness Type Double Patenting-Second reference***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re*

*Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-14, and 18 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 6,479,051, in view of Falsen (International Journal of Systematic Bacteriology, 1999, 217-221) and Nugent et al., (J Clin Microbiol. 1991 29:297-301).

Claims 1-17 of U.S. Patent No. 6,479,051, are drawn to a method for establishing a healthy urogenital bacterial flora in females throughout life, a method of treating or preventing urogenital infections, a method of improving or restoring the urogenital microenvironment by administering a therapeutically effective amount of at least one probiotic organism selected from the group consisting of *Lactobacillus rhamnosus* GR-1, *L. rhamnosus* GR-2, *L. rhamnosus* GR-3, *L. rhamnosus* GR-4, *L. rhamnosus* RC-17, *L. rhamnosus* RC-12, *L. jensenii* RC-11, *L. acidophilus*, *L. acidophilus* RC-14, *L. plantarum* RC-20, *L. plantarum* RC-6, *L. fermentum* A-60, *L. fermentum* B-54 and milk or a portion thereof as a pharmaceutically acceptable carrier.

The claims of the Patent No. 6,479,051 differ from the instantly claimed invention by no citing the specific strain of *L. iners*.

However, at the effective filing date of the present application, Falsen et al., (International Journal of Systematic Bacteriology, 1999, 217-221) is an exemplified prior art that teaches the use of *Lactobacillus* as probiotics (i.e., dietary adjuncts for man and animal). Moreover, Falsen et al., teaches the discovery of a new species of the genus *Lactobacillus*: *Lactobacillus iners*, isolated from human clinical specimens of the vagina (p. 221, col. 1). Similarly, Nugent et al., teach the correlation between a healthy vaginal tract and dominance of lactobacilli (p. 298, col. 2, and Table 1).

Accordingly, in view of the benefits of using the numerous species of the genus *Lactobacillus* in a method for establishing a healthy urogenital flora by administration of a therapeutically effective amount of a specific strain of *Lactobacillus* as taught by the U.S. Patent No. 6,479,051, it would have been obvious to use the newly isolated species of *Lactobacillus iners*, particularly because Falsen et al., teach that *Lactobacilli* are used as probiotics and the new isolated *Lactobacillus iners* is present in the vagina. Moreover, Nugent discloses a correlation of healthy vaginal tract (e.g., lack of symptoms and signs of disease). One of ordinary skill in the art would have been motivated to generate a healthy urogenital bacterial flora in females by administration of *lactobacillus iners* present in a healthy vagina with a reasonable expectation of success particularly in view of the totality of the prior art at the time the invention was made.

Claims 1-14, and 17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 6,479,051, in view of Falsen (International Journal of Systematic Bacteriology, 1999, 217-221) and Nugent et al., (J Clin

Microbiol. 1991 29:297-301) and further in view of Gibson et al., (Gastroenterology, 1995, 975-82) .

Claims 1-17 of U.S. Patent No. 6,479,051, are drawn to a method for establishing a healthy urogenital bacterial flora in females throughout life, a method of treating or preventing urogenital infections, a method of improving or restoring the urogenital microenvironment by administering a therapeutically effective amount of at least one probiotic organism selected from the group consisting of *Lactobacillus rhamnosus* GR-1 , *L. rhamnosus* GR-2, *L. rhamnosus* GR-3, *L. rhamnosus* GR-4, *L. rhamnosus* RC-17, *L. rhamnosus* RC-12, *L. jensenii* RC-11, *L. acidophilus*, *L. acidophilus* RC-14 , *L. plantarum* RC-20, *L. plantarum* RC-6, *L. fermentum* A-60, *L. fermentum* B-54 and milk or a portion thereof as a pharmaceutically acceptable carrier.

The claims of the Patent No. 6,479,051 differ from the instantly claimed invention by not citing the specific strain of *L. iners*.

However, at the effective filing date of the present application, Falsen et al., (International Journal of Systematic Bacteriology, 1999, 217-221) is an exemplified prior art that teaches the use of *Lactobacillus* as probiotics (i.e., dietary adjuncts for man and animal). Moreover, Falsen et al., teaches the discovery of a new species of the genus *Lactobacillus*: *Lactobacillus iners*, isolated from human clinical specimens of human clinical specimens of a vagina (p. 221, col. 1). Similarly, Nugent et al., teach the correlation between a healthy vaginal tract and dominance of lactobacilli (p. 298, col. 2, and Table 1).

Neither U.S. Patent No. 6,479,051, or Falsen and Nugent teach the use of inulin as a prebiotic.

At the effective filing date of the present application, Gibson et al., (International Journal of Systematic Bacteriology, 1999, 217-221) is an exemplified prior art that teaches the use of inulin as naturally occurring indigestible carbohydrates that selectively stimulated the growth of species of Bifidobacterium in the gastrointestinal tract (p. 975). Moreover, Gibson teaches that addition dietary of inulin led to Bifidobacterium as the predominant genus of the feces and thus to a colonic healthier microflora.

Accordingly, in view of the benefits of using the numerous species of the genus *Lactobacillus* in a method for establishing a healthy urogenital flora by administration of a therapeutically effective amount of a specific strain of *Lactobacillus*, it would have been obvious to use the newly isolated species of *Lactobacillus iners*, particularly because Falsen et al., teach that *Lactobacilli* are use as probiotics and the new isolated *Lactobacillus iners* is present in the vagina. Moreover, Nugent discloses a correlation of healthy vaginal tract (e.g., lack of symptoms and sings of disease). Further, it would have been obvious to use inulin as a prebiotic in a method wherein a second probiotic is of the genus Bifidobacterium, particularly because Gibson teaches that dietary inulin lead to predominance of Bifidobacterium in the gastrointestinal tract. One of ordinary skill in the art would have been motivated to generate a healthy urogenital bacterial flora in females by administration of *lactobacillus iners* with a reasonable expectation of success particularly in view of the totality of the prior art at the time the invention was made.

Claims 1-15 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 5, 6, 7, 8, 9 and 10 of U.S. Patent No.

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6,180,100, in view of Falsen (International Journal of Systematic Bacteriology, 1999, 217-221) and Nugent et al., (J Clin Microbiol. 1991 29:297-301).

Claims 1, 2, 5, 6, 7, 8, 9 and 10 of U.S. Patent No. 6,180,100, are drawn to a method for improving or restoring the urogenital microenvironment, and methods for preventing colonization of pathogenic bacteria on epithelial surfaces of a urogenital tract in a mammal by administering a therapeutically effective amount of at least one probiotic organism selected from the group consisting of *Lactobacillus rhamnosus* GR-1, *L. rhamnosus* GR-2, *L. rhamnosus* GR-3, *L. rhamnosus* GR-4, *L. rhamnosus* RC-17, *L. rhamnosus* RC-12, *L. jensenii* RC-11, *L. acidophilus*, *L. acidophilus* RC-14, *L. plantarum* RC-20, *L. plantarum* RC-6, *L. fermentum* A-60, *L. fermentum* B-54 and a composition comprising *Lactobacillus*.

The claims of the Patent No. 6,180,100 differ from the instantly claimed invention by not citing the specific strain of *L. iners*.

However, at the effective filing date of the present application, Falsen et al., (International Journal of Systematic Bacteriology, 1999, 217-221) is an exemplified prior art that teaches the use of *Lactobacillus* as probiotics (i.e., dietary adjuncts for man and animal). Moreover, Falsen et al., teaches the discovery of a new species of the genus *Lactobacillus*: *Lactobacillus iners*, isolated from human clinical specimens of a vagina (p. 221, col. 1). Similarly, Nugent et al., teach the correlation between a healthy vaginal tract and dominance of lactobacilli (p. 298, col. 2, and Table 1).

Accordingly, in view of the benefits of using the numerous species of the genus *Lactobacillus* in a method for establishing a healthy urogenital flora by administration of a therapeutically effective amount as taught by U.S. Patent No. 6,180,100, it would have been

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obvious to use the newly isolated species of *Lactobacillus iners*, particularly because Falsen et al., teach that *Lactobacilli* are used as probiotics and the new isolated *Lactobacillus iners* is present in the vagina. Moreover, Nugent discloses a correlation of healthy vaginal tract (e.g., lack of symptoms and signs of disease). One of ordinary skill in the art would have been motivated to generate a healthy urogenital bacterial flora in females by administration of *Lactobacillus iners* with a reasonable expectation of success particularly in view of the totality of the prior art at the time the invention was made.

#### Conclusion

Claims 1-19 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maria Leavitt whose telephone number is 571-272-1085. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1636; Central Fax No. (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the



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Maria Leavitt, PhD  
Patent Examiner P/1633  
Remsen 2B55  
Phone: 571-272-1085

ANNE M. WEHBE' PH.D  
PRIMARY EXAMINER

A handwritten signature in black ink, appearing to be 'AW', written over the printed name of the examiner.